REMARKS

Claims 1-5, 20-24, 26-37, 39, 40, 42, 43, 54-56 and 59-68 are pending in the present application. By virtue of this response, claims 20, 26, 31, 32, 35 and 39 have been amended, claim 66 cancelled, and new claims 69-73 have been added.

The amendments of claims 20 and 31 are made solely to correct clerical errors. Support for the amendment of claim 26 is found in the specification, *inter alia*, on page 66, lines 19-21; Figure 23 and SEQ ID NO:33. Support for the amendment of claim 32 is found in the specification, *inter alia*, on page 68, lines 12-21; and page 72, line 21 to page 73, line 2. Support for the amendment of claim 35 is found in the specification, *inter alia*, on page 71, lines 15-16. Support for the amendment of claim 39 is found in the specification, *inter alia*, on page 63, line 25 to page 64, line 7; page 64, lines 21 to page 65, line 8; and page 89, line 19 to page 90, line 5. Support for new claim 69 is found in the specification, *inter alia*, on page 29, line 24 to page 30, line 2; and SEQ ID NO:2. Support for new claim 70 is found in the specification, *inter alia*, on page 29, line 24 to page 30, line 2; and SEQ ID NO:4. Support for new claim 71 is found in the specification, *inter alia*, on page 68, lines 12-21; and page 72, line 21 to page 73, line 2. Support for new claim 72 is found in the specification, *inter alia*, on page 71, lines 16-19. Support for new claim 73 is found in original claim 35 and in the specification, *inter alia*, on page 71, lines 16-19.

Attached hereto is a marked up version of the changes made to the claims by the current amendment with additions underlined and deletions bracketed. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**".

Applicants reiterate their request for rejoinder of presently excluded method claims, to the extent that they incorporate all the limitations of the product claims. The Examiner has indicated that once allowable product claims are identified, then method claims which incorporate all the limitations of the product claims and which do not present any new issues

may be rejoined. Office Action of March 31, 1999, page 2. Applicants note that the Office's training document for rejoinder ("Training Materials for Treatment of Product and Process Claims in Light of *In re Brouwer* and *In re Ochiai* and 35 USC 103(b)", dated July 25, 1996) states that "[I]f applicant elects claims directed to the product, and the product is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product will be rejoined." Pages 3-4.

With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and /or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional application.

Claim objections

With this Amendment, the appropriate correction of the spelling of "complementarity" has been made. Thus, this objection should be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 26 and 35 stand rejected as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

With respect to claim 26, Applicants respectfully disagree that it is not clear what is meant by the word "tandem repeat sequence." The specification amply describes this term (see, for example, page 66, lines 19-21, Figure 23 and SEQ ID NO:33), and one of skill in the art would understand what is meant by this phrase. However, in the interest of expediting prosecution, claim 26 has been amended to recite "wherein said tandem repeat sequence is contained in SEQ ID NO:33." Thus, Applicants respectfully request withdrawal of this rejection.

Claim 35 is rejected as allegedly indefinite for reciting "humanized antibody" because only murine CDRs are recited, and that the claim fails to include reference to human framework regions or human constant regions.

Applicants respectfully traverse.

The claim is directed to a humanized antibody that is able to stimulate a specific immune response against human milk fat globule. Applicants submit that one of skill in the art understands what is meant by a "humanized" antibody, and would readily recognize the components that comprise a humanized antibody that is operable as claimed. Applicants further submit that one of skill in the art would understand that a humanized antibody can, but does not necessarily, include *human* framework regions and/or *human* constant regions.

Applicants also note that despite the Examiner's contentions, a number of U.S. patents have issued in which claims directed to humanized antibodies do not include a reference to human framework regions or human constant regions, for example U.S. Patent Nos. 6,054,297 and 6,056,957.

However, in the interest of expediting prosecution and solely for clarification, Applicants have amended claim 35 to recite the limitation "a constant region that is a human sequence." Applicants also note that new claims 72 and 73 have been added.

Concerning deposit of biological materials

Applicants acknowledge with appreciation the withdrawal of the rejection of claims 1-5, 20-22, 26, 35-37, 39, 40, 42-43, 54-56 and 59-61 under §112, first paragraph. In view of this withdrawal, the Office has deemed the deposit information to be complete, and Applicants therefore will not address the Examiner's arguments set forth in subparagraphs a & b of page 4 of the Office Action.

Rejection under U.S.C. § 112, first paragraph

Claims 39, 62 and 63 stand rejected because the specification, while allegedly being enabling for polypeptides which contain all six CDRS of 11D10, allegedly does not reasonably provide enablement for polypeptides which contain only one of the six CDRS.

Claim 39 has been amended to recite "an immunoglobulin variable region containing three light chain complementarity determining regions (CDRs) of antibody 11D10, or an immunoglobulin variable region containing three heavy chain CDRs of antibody 11D10." Applicants note that the Examiner's previous rejection of claims 20-24, 26, 35-36 and 61 on a similar ground was withdrawn following amendment of the claims to recite that the polypeptide comprises three light chain CDRs or three heavy chain CDRs. Office Action dated March 31, 1999 (paper no. 19), pages 7-10. Thus, Applicants respectfully request withdrawal of the rejection of claims 39, 62 and 63.

Rejection under U.S.C. § 112, second paragraph

Claims 39, 62 and 63 are rejected as allegedly failing to set forth the subject matter which applicants regard as their invention.

As discussed above, claim 39 has been amended to recite "an immunoglobulin variable region containing three light chain complementarity determining regions (CDRs) of antibody 11D10, or an immunoglobulin variable region containing three heavy chain CDRs of antibody 11D10." Applicants believe this fully addresses the Examiner's concern stated in paragraph 10 of the Office Action. Thus, Applicants respectfully request withdrawal of the rejection of claims 39, 62 and 63.

Rejection under 35 U.S.C. § 102(b)

Claims 1-5, 20-27, 31-33, 36, 37, 39-40, 42-43, 55-56 and 59-68 stand rejected as allegedly being anticipated by any of:

i. Chatterjee (*Antigen and Antibody Molecular Engineering*, (1994));

ii. Chatterjee et al. (*Cancer Immunol Immunther*, (1994), Vol 34:75-82);

iii. Chakraborty et al. (*Proc Am Assoc Cancer Res*, (1994), Abstract 2963);

iv. Chakraboty et al. (*Immunotherapy*, (1995), Vol 18(2):95-103); or

v. Chakraboty et al. (*Cancer Research*, (4/1/1995), Vol 55:1525-1530).

Applicants respectfully traverse this rejection.

The Examiner alleges that the 37 CFR 1.132 declarations submitted 10/4/99 by M. Chatterjee, K. Foon and S. Chatterjee are not persuasive[1] because the role of Dr. Kohler in the invention was not accounted for, and that the declarants "merely state that he did not participate in generating or characterizing 11D10 . . ." Office Action, page 7. Applicants respectfully submit that this statement in M. Chatterjee's declaration was sufficient, and that its sufficiency was acknowledged by the Examiner in the previous Office Action (dated March 31, 1999; paper no. 19; pages 13-14, subparagraph d)[2].

Applicants further submit that the Examiner's argument is irrelevant for a rejection under §102(b), as §102(b) applies irrespective of the identity of inventors. M. Chatterjee's declaration is irrelevant for §102(b) purposes. The declaration was submitted to address a question of inventive entity (raised by the Examiner during telephone interviews on July 14 and September 25, 1998) with respect to co-authors of certain references.

The Examiner alleges that the declarations attempt to overcome a 102(b) rejection by stating that the 11D10 hybridoma and antibody were not publicly available, and notes that 102(b) also bars inventions which are described in a written publication. Applicants have addressed this very issue in the response dated September 30, 1999 (paper no. 20) and presented original

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[1] The Examiner also refers to considering the declarations of Drs. S. Chatterjee and K. Foon; however, only Dr. Malaya Chatterjee's declaration addresses the inventorship issue.

[2] The Examiner stated that "[t]he declaration persuasively accounts for the role of Ceriani, Kohler and Sherratt in the invention of 11D10 such that there is no reason to believe that they contributed to the invention of 11D10." The Examiner's silence with respect to Kohler's role was implicit approval of the sufficiency of the declaration on this point.

arguments in the response dated October 8, 1998. The Examiner has not acknowledged those arguments and declarations, and appears not to have yet considered them. Applicants have pointed out, and herein reiterate, that none of the cited publications anticipates the pending claims because (a) the cited references are not enabling because they do not teach and/or enable obtaining 11D10 antibody, and do not disclose the amino acid sequence or DNA coding sequence for the variable regions of 11D10, and thus cannot be used as a prior art reference; and (b) neither 11D10 nor the hybridoma producing 11D10 were made available to the public. With respect to the references being non-enabling, Applicants' previous response (dated October 8, 1998), discussed in detail the mechanism of antibody formation as well as the uniqueness of the 11D10 sequence (which was not disclosed in any of the references).

The Examiner makes no reference to these arguments that are on the record. Moreover, Applicants respectfully point out that the Examiner has already considered virtually identical facts and arguments in two other related cases, one of which has matured into an issued U.S. patent (5,612,030), and the other allowed (U.S. Ser. No. 08/579,940). Applicants respectfully submit that ample reasons have been provided as to why none of the cited references anticipates the invention, and request that this rejection be withdrawn.

The declarations of Drs. Malaya Chatterjee, Sunil Chatterjee, and Kenneth Foon, addressing lack of public availability of 11D10, have also been discussed in the previous response (dated October 8, 1998).

With respect to Chakraborty et al., *Cancer Research* (4/1/1995), Vol. 55:1525-1530 (reference v on page 6 of Office Action), the Examiner alleges that the reference recites a murine anti-idiotype antibody named 11D10, and that it reads upon the claims. Applicants respectfully submit that this is an improper §102(b) reference as it was published within one year of the effective filing date of the instant application. The publication date of the reference is April 1, 1995, which is less than a year from the effective filing date of the instant application (based on claim of priority back to Provisional Application No. 60/031,306 (formerly U.S. Serial No.

08/575,762, filed December 20, 1995) and Provisional Application No. 60/035,345 (formerly U.S. Serial No. 08/591,965, filed January 29, 1996)). Applicants therefore request withdrawal of this reference as a basis of rejection, and respectfully request withdrawal of said rejection.

The role/contribution of the authors of the Chakraborty et al. reference (ref. v) has been addressed in the Declaration of Malaya Bhattacharya-Chatterjee (submitted September 30, 1999). Therefore, Applicants respectfully point out that this reference is not available as a §102(a) or §102(f) reference.

The Examiner also maintains that, with respect to reference (v), the publication policy of the *Cancer Research* journal requires that by publishing in the journal the authors agreed to make freely available their hybridoma and 11D10 antibody, and that the declaration of 10/4/1999 does not explain how the antibody was not publicly available when "this was a requirement" of the journal. Office Action, page 7. Applicants respectfully submit that the journal merely has a *policy* that authors agree to make freely available to others materials used in reported research, but does not *require* that the authors do so. Nonetheless, as discussed above, this reference is unavailable as §102 art.

In view of the above, Applicants respectfully request withdrawal of the rejection of claims 1-5, 20-27, 31-33, 36, 37, 39-40, 42-43, 55-56 and 59-68.

Rejection under 35 U.S.C. 102(f)

Claims 1-5, 20-27, 31-33, 36-37, 39-40, 42-43, 55-56 and 59-68 stand rejected under §102(f) as by any of Chatterjee et al. (*Antigen and Antibody Molecular Engineering* (1994)), Chatterjee et al. (*Cancer Immunol Immuntherapy* (1994), 34:75-82), Chakraborty et al (*Proc Am Assoc Cancer Res* (1994), Abstract 2963) or Chakraborty et al (*Immunotherapy Vol,* (1995), 18(2):95-103) and Chakraborty et al (*Cancer Research* (1995), 55:1525-1530), allegedly because the inventors did not invent the work sought to be patented.

Applicants respectfully traverse.

The Examiner asserts that the 37 CFR 1.132 declaration submitted 10/4/1999[3] was not persuasive because it allegedly fails to account for the role Dr. Kohler had in the invention, and that it merely states that he did not participate in generating or characterizing 11D10. Office Action, pages 8-9. A declaration stating that H. Kohler "did not participate in any way with the generation or characterization of 11D10" (Declaration of Malaya Battacharya-Chatterjee submitted September 30, 1999; page 6) is sufficient for overcoming a §102(f) rejection, as acknowledged by the Examiner in the previous Office Action (dated March 31, 1999; paper no. 19; pages 13-14, subparagraph d). Further, the statement in the declaration answers the question of whether Dr. Kohler is an inventor. No other information is necessary or required. Furthermore, the role/contribution of the authors of the newly applied reference (Chakraborty et al., ref. v, page 6 of Office Action) has been addressed in the same declaration. Therefore, Applicants respectfully submit that the Examiner's concern regarding the role/contribution of authors named in the cited references has been fully addressed with respect to the instant rejection under §102(f).

In view of the above, Applicants respectfully request the withdrawal of the rejection of claims 1-5, 20-27, 31-33, 36-37, 39-40, 42-43, 55-56 and 59-68.

Rejection under 35 U.S.C. §102(e)

Applicants acknowledge with appreciation the withdrawal of the rejection of claims 20, 22, 24, 26, 33-36, 39, 42, 56 and 61 as previously alleged to be anticipated by Gourlie et al.

Applicants acknowledge with appreciation the withdrawal of the rejection of claims 20, 21, 23, 26, 33-36, 39, 42, 56 and 61 as previously alleged to be anticipated by Bendig et al.

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[3] The Examiner also refers to considering the declarations of Drs. S. Chatterjee and K. Foon; however, only Dr. Malaya Chatterjee's declaration addresses the inventorship issue.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

MURINE ANTI-IDIOTYPE ANTIBODY 11D10 AND METHODS OF USE THEREOF
BY: Klaus RAJEWSKY AND Yong-Rui ZOU

In the claims

Claim 66 has been cancelled.

Claims 69-73 have been added.

Claims 20, 26, 31-32, 35 and 39 have been amended as follows:

20. (Thrice amended) A polypeptide having immunological activity of anti-idiotype antibody 11D10, wherein the polypeptide comprises an immunoglobulin variable region containing three light chain [complementary] complementarity determining regions (CDRs) of antibody 11D10, or an immunoglobulin variable region containing three [light] heavy chain CDRs of antibody 11D10, wherein the light chain variable region amino acid sequence is contained in an antibody produced by a hybridoma cell line designated ATCC NO. HB 12020 or progeny thereof, and wherein the heavy chain variable region amino acid sequence is contained in an antibody produced by a hybridoma cell line designated ATCC NO. HB 12020 or progeny thereof, and wherein the immunological activity of the polypeptide is an ability to stimulate a specific immune response against human milk fat globule (HMFG).

26. (Twice Amended) The polypeptide of claim 20, wherein the polypeptide contains a sequence of at least 2 contiguous amino acids which are identical in forward or reverse orientation to 2 contiguous amino acids of a tandem repeat sequence in human mucin from human milk fat globule, wherein said tandem repeat sequence is contained in SEQ ID NO:33.

31. (Twice amended) The fusion polypeptide of claim 27, which comprises three CDRs from the light chain variable region of 11D10 and [3] three CDRs from the heavy chain variable region of 11D10[, wherein the CDRs from 11D10 are contained in an antibody produced by a hybridoma cell line designated ATCC NO. HB 12020 or progeny thereof].

32. (Twice amended) The fusion polypeptide of claim 31, wherein the [contiguous amino acids of SEQUENCE ID NO:2 and the contiguous amino acids of SEQUENCE ID NO:4] three CDRs from the light chain variable region of 11D10 and the three CDRs from the heavy chain variable region of 11D10 are linked by a linker polypeptide of about 5 to 20 amino acids.

35. (Twice Amended) A humanized antibody comprising three CDRs from the light chain variable region of 11D10, [and] three CDRs from the heavy chain variable region of 11D10, and a constant region that is a human sequence, wherein the humanized antibody is able to stimulate a specific immune response against human milk fat globule (HMFG), wherein the light chain variable region amino acid sequence is contained in an antibody produced by a hybridoma cell line designated ATCC No. HB 12020 or progeny thereof, and wherein the heavy chain variable region amino acid sequence is contained in an antibody produced by a hybridoma cell line designated ATCC No. HB 12020 or progeny thereof[, and wherein the immunological activity of the polypeptide is an ability to stimulate a specific immune response against human milk fat globule (HMFG)].

39. (Thrice amended) A composition comprising a pharmaceutically acceptable excipient and a polypeptide having immunological activity of anti-idiotype antibody 11D10, wherein the polypeptide comprises [at least one complementarity determining region (CDR) from the light or heavy chain variable region of 11D10] an immunoglobulin variable region containing three light chain complementarity determining regions (CDRs) of antibody 11D10, or

an immunoglobulin variable region containing three heavy chain CDRs of antibody 11D10, wherein the light chain variable region amino acid sequence is contained in an antibody produced by a hybridoma cell line designated ATCC NO. HB 12020 or progeny thereof, and wherein the heavy chain variable region amino acid sequence is contained in an antibody produced by a hybridoma cell line designated ATCC NO. HB 12020 or progeny thereof, and wherein the immunological activity of the polypeptide is an ability to stimulate a specific immune response against human milk fat globule (HMFG).

CONCLUSION

Applicants believe they have addressed all issues raised by the Office and that the claims are in condition for allowance, which is respectfully requested. If the Examiner wishes to discuss this application or provide comments, she is invited to telephone Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 304142000321. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: March 26, 2001 By: _____

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Limited Recognition Under 37 C.F.R. §10.9(b)
(copy of certificate attached)

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